DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date: 12/03/02

From: Gloria Chang, IDS/Pharmacist, Division of Standards and Labeling Regulations, Office of Nutritional Products, Labeling and Dietary Supplements, HFS-820

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

New Dietary Ingredient: BioVitaflu/BioVitabronch (Vitex negundo, L)

Firm: Kelatron Corp.

Date Received by FDA: 2/11/02

90-Day Date: 5/12/02

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached correspondence for the aforementioned dietary ingredient should be placed on public display in docket number 95S-0316 as soon possible. Thank you for your assistance.

Gloria Chang

Gloria Chang, IDS/Pharmacist

Attachments

95S-0316

RPT117

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD

APR 26 2002

Mary Ann Coral-Amasifuen
Kelatron Corporation World Headquarters
1675 West 2750 South
Ogden, Utah 84401

Dear Ms. Coral-Amasifuen:

This is in response to four separate notifications you submitted pursuant to 21 U.S.C. 350b(a)(2). All four notifications were received by the Food and Drug Administration (FDA) on January 3, 2002, followed by an addendum dated January 10, 2002. In follow up, we contacted you by telephone on January 14, 2002 notifying you that the notifications were incomplete (see background of follow up below). Subsequently, you sent addendums dated January 18, and February 5, 2002. We received your last addendum for your notifications dated February 5, 2002 on February 11, 2002. Therefore, the effective filing date for all four notifications is February 11, 2002.

As noted above, we contacted you by telephone on January 14, 2002 notifying you that the notifications were incomplete in that they did not contain levels of the dietary ingredients, conditions of use, or copies of the full-text journal articles corresponding to the abstracts you sent us. We explained that the requested information would have to be submitted in triplicate (3 copies) if we were to consider these references in our review. On January 24, 2002, we called you again and left a message that the addendums that you sent dated January 18, 2002, did not contain the levels of the new dietary ingredients as requested.

Each notification concerned a different botanical that you assert is a new dietary ingredient. The botanicals are listed below by the Latin binomial name, plant form, and product name as stated in your notifications.

Vitex negundo L. (pure leaf powder) -- BioVitaflu/BioVitabronch
Blumea balsamifera L. (pure leaf power) -- BioRenal
Mormadica charantia L.- Makiling v. (pure leaf powder) -- BioDiamed
Lagerstroemia specious L. (pure leaf powder) -- BioDiamend

The law at 21 U.S.C. 350b(a)(2) requires that a manufacturer or distributor submit certain information to FDA at least 75 days before a new dietary ingredient or a dietary supplement containing it is introduced or delivered for introduction into interstate commerce. This information must include the basis on which the manufacturer or distributor has concluded that the new dietary ingredient or a dietary supplement containing it will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under 21 U.S.C. 350b(a)(2), there must be a history of use or other evidence of safety establishing that the dietary ingredient, when used under the conditions recommended or suggested in the product's labeling, will reasonably be expected

to be safe. If this requirement is not met, the new dietary ingredient or dietary supplement containing it is deemed to be adulterated under 21 U.S.C. 342(f)(1)(B), because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

FDA has considered the information in your notification and has several significant concerns. Based on the information in your notification for all four botanical ingredients, FDA has determined that the information submitted suggests that the intended uses imply or represent treatment of disease. The following are examples.

- The botanical ingredient *Vitex negundo* L., the product name "BioVitaflu/BioVitabronch" implies a recognizable disease condition, the "flu". FDA considers a brand name that includes a disease name or a clearly recognizable derivation of a disease name to be a disease claim. (See 21 CFR 101.93(g)(2)(iv)(A).)
- Under the conditions of use for the botanical ingredient *Blumea balsamifera* L. (BioRenal) you state that BioRenal might be effective as a diuretic and as an anti-urolithiasis agent (chronic formation of kidney stones).
- Under the conditions of use for the botanical ingredient *Mormadica charantia* L.-Makiling v. (BioDiamed) you state that the recommended use is that it may be helpful for blood sugar regulation and type II diabetes mellitus.
- Under the conditions of use for the botanical ingredient *Lagerstroemia specious* L.-(BioDiamend) you state that clinical trials indicated that BioDiamend may have some blood sugar lowering properties in vivo and therefore the recommended use is that it may be helpful for blood sugar regulation and type II diabetes mellitus.

Please be advised that any representation that a product is intended for the diagnosis, cure, mitigation, treatment or prevention of disease in man or animals suggests that it is a drug, as defined in 21 U.S.C. § 321(g)(1)(B), and would be subject to regulation under the drug provisions of the Federal Food, Drug and Cosmetic Act. All drugs must be approved by FDA before they can be marketed in the United States. If you wish to market your products as drugs, you should contact FDA's Center for Drug Evaluation and Research (CDER), Office of Compliance, HFD-310, 7520 Standish Place, Rockville, Maryland 20855.

FDA also has concerns about the evidence on which you rely to support your conclusion that the four botanical ingredients in your notifications will be reasonably expected to be safe for the suggested or intended uses.

Much of the history of use information you submitted appears to be selected pages printed from commercial magazines or promotional literature. Some of the sources of these articles were not identified nor were the specific ingredients in your notifications mentioned in the articles. These articles primarily focus on anecdotal use for disease conditions and do not address safety. The statements in these articles cannot be validated and are not corroborated

by scientific data. Although requested, you did not provide us with photostatic copies or reprints of all of the abstracts or the complete reference citation for what appears to be an excerpt from a reference book. Consequently, those abstracts and excerpts were not considered in our review.

We are also unsure if the botanical ingredients described in some of the scientific literature were the same as those described in your notifications. Further, we are not sure if the specific genus, species, and author citations are correct for two of the botanical ingredients. Although we searched a number of botanical databases, we could not find the specific Latin binomial names *Mormadica charantia* L. and *Lagerstroemia specious* L as stated in your notifications. We are aware of the Latin binomial names *Momordica charantia* L. or *Momordica charantia* Linn. and *Lagerstroemia speciosa* L. or *Lagerstroemia speciosa* (L.) Pers. However, when referring to your botanical ingredients in this letter, we will be using the Latin binomial names as stated in your notifications.

We also have concerns regarding the scientific information that was submitted. Most of the scientific articles and unpublished reports in your notifications primarily address use of the study ingredients as drugs to treat specific disease conditions and do not provide adequate evidence of the safe use of the specific ingredient. Also, it was not clear if the ingredients used in some of the studies were the same ingredients (genus, species, and author citation), the same part of the plant, or the levels per serving dose, as those stated in your notifications.

In your notification on *Vitex negundo* L (BioFlu/Bio Vitabronch), you submitted a summary of an unpublished, uncontrolled, open label study evaluating the safety and efficacy of *Vitex negundo* L (Lagundi) tablets as an antitussive agent. The trial titled Section 5.2:Phase II Clinical Trial was conducted from January to December 1984. Twenty-five subjects were enrolled, 20 children and 5 adults. Subjects were described as having acute asthma (n=4) or upper-respiratory, non-bacterial infection (n=21). There was a single concluding statement of safety that noted that there were no untoward side effects noted or volunteered. No details or specific data on safety was provided. We also note that the actual dose level in each tablet was not stated. Further, subjects with present or past disease conditions were explicitly not enrolled in the trial as stated in the exclusion criteria of the study. This is of particular concern since under your conditions of use there are no recommendations to restrict its use in persons with pre-existing disease conditions.

In the report of a randomized study comparing lagundi (15 mg/kg taken every 8 hours for 3 days) to theophylline (3 mg/kg taken every 8 hours for 3 days) for the treatment of acute asthmatic exacerbation (a disease condition), forty-three subjects were enrolled, however; 3 subjects dropped out after 24 hours. Twenty of the subjects were exposed to lagundi. The analysis was done on forty subjects, 6 males and 34 females. For almost all outcome measures the theophylline group was superior to the lagundi group. Adverse events were noted for 8 theophylline subjects and 5 in the lagundi group. In the lagundi group, the side effects noted were emesis (2 cases), palmar desquamation (2 cases) and increased urinary frequency (1 case). The author did not comment on the subjects that developed palmar

desquamation. The author also expressed concerns about the inadequacy of this study and recommended further evaluation and investigation of lagundi.

We also have concerns regarding the short exposure time to lagundi. The total clinical exposure cited as a safety database consists of only approximately 45 individuals with only a maximum exposure to lagundi of 72 hours. Considering that you did not indicate any limitation or duration of use, these studies do not address chronic use or long term use. Further, we have concerns that subpopulations with present or past medical conditions that were excluded in the study, were not recommended for exclusion under your conditions of use. Accordingly, the study cannot support the conclusion that lagundi is reasonably expected to be safe if marketed as a new dietary ingredient for the intended or suggested use.

In the notification for *Blumea balsamifer* L. (BioRenal), you submitted sections of a larger unpublished study labeled as "7.0 CLINICAL TRIALS." The subsections are; 7.1 "Phase I: Sambong Tablet as Diuretic", 7.2 "Phase II:Clinical Trial of Sambong Tablet as Diuretic," 7.3 "Phase II:Sambong Tablet as anti-urolithiasis," 7.4, "Phase III clinical Trial of *Blumea balsamifer* L (Sambong) tablet in the treatment of urinary tract stone: a randomized double-blind placebo-controlled study", and 7.5 "Extended Phase III Open Trial of *Blumea balsamifer* L (Sambong) for the treatment of urinary tract stones."

All of the studies were small. Overall, 59 subjects were exposed to Sambong across all 5 studies. Exposure time ranged from 2 days to a maximum of approximately 6 weeks. Most of the exposures were less than 6 weeks.

In the studies for diuretic use, we have the following specific comments. No mechanism for the diuretic activity was ascertained, yet based on the conclusions reached that the diuretic effect of Sambong was comparable to thiazide diuretics, Sambong use may pose a safety risk in a normal population or in a subpopulation who may be also using other diuretics. The studies did not sufficiently address safety. Based on the conclusions in the study that Sambong tablets produced statistically significant diuresis and chloriuresis comparable to hydrochlorthiazide given at 50 mg in 2 divided doses, we have concerns that this may pose an electrolyte imbalance risk in normal populations or in a subpopulation with certain present or past medical conditions. Your recommended conditions of use only excluded use in lactating or pregnant women. Your recommended use in adults 18 years old and over neither included instructions on limitations or duration of use nor excluded use for any other populations that may be at risk either for using diuretics or due to concurrent use of other diuretic agents.

In addition, we have concerns regarding the implied use of BioRenal to treat or prevent kidney stones, a disease condition. We have significant safety concerns that consumers will not be able to self diagnose this specific disease condition and that prolonging medical treatment may lead to more serious health consequences.

In your notification for *Mormadica charantia* L.- Makiling v. (BioDiamed), the only full text journal article, was a general summary on the anti-diabetic properties and phytochemistry of a

botanical *Momordica charantia* L. Please note the difference in the Latin binomial names for your botanical ingredient and the botanical cited in the article. The article primarily focuses on general efficacy, and not the safety of the seeds or juice of the plant. It does not address the specific plant part or form (the pure leaf powder) or the serving levels as that of your ingredient. Further, the *in vivo* animal studies information presented a general overview of referenced toxicity studies and focused primarily on the juice or extracts of Karela. You did not provide the referenced full text journal articles in your notification. We are unsure if Karela is the same plant source or plant form as your ingredient. Nonetheless, the animal toxicity information did not provide any dosing levels used nor did it address the specific plant form described in your notification.

Thus, we conclude that the evidence of safety from the article was minimal or lacking and no conclusions of safety can be drawn from the report. We also cannot draw any safety conclusions from the other published report on the hyperglycemic activity of polypeptides of a plant source (fruit, seeds, and tissue). That report focuses on a peptide isolated from the seeds and tissue of a botanical variety, *Momordica charantia* Linn. and does not describe the specific plant part (pure dried leaf powder) described in your notification. Further, the report primarily addresses hypoglycemic activity of the peptide and the only safety information is a statement that referenced a study using a polypeptide-p-ZnCl in three juvenile patients. A photostatic copy or reprint of the full published text of that citation reference was not included in your submission. Thus, no conclusions regarding safety can be drawn from the report.

In your notification for *Lagerstroemia specious* L., the study submitted appears to be an unpublished trial titled "The Clinical Study on the Water Extract of Leaves of *Lagerstroemia specious* L for Mild Cases of Diabetes Mellitus." Twenty-four subjects over the age of 20 years were studied. There is very little information on safety in this report and it is unclear if the study was a single or double-blinded study, a critical concern in safety analysis. The only statement regarding safety was a statement that all 24 subjects did not have any adverse effects. In the absence of detailed safety data and the small size of the study, there is very little evidence to conclude that the ingredient can be reasonably expected to be safe for its intended or suggested use.

Overall, the evidence of safety provided for all four of the dietary ingredients submitted is either minimal or lacking. All of the supporting studies were of a short duration, without any evidence demonstrating safety with chronic exposure. You indicated that under conditions of use these ingredients in general, were to be recommended for use in adults (18 and over) and were not to be used by lactating or pregnant women. However, the study exclusion criteria specifically excluded subpopulations with certain medical conditions from the studies. This may be of particular concern, because under your conditions of use you did not indicate any limit or duration of use for the four botanicals and persons excluded from clinical trials are not excluded under your recommended conditions of use.

We have determined that the history of use information you submitted in all four of your notifications has limited utility in evaluating the safety of these ingredients if marketed as

dietary supplements. In conclusion, the information in your notifications does not provide an adequate basis to conclude that *Vitex negundo* L., *Blumea balsamifera* L., *Mormadica charantia* L.- Makiling v., and *Lagerstroemia specious* L. are reasonably expected to be safe when used under the recommended or suggested conditions of use. Therefore, any product containing any of the botanicals listed in your notifications as *Vitex negundo* L., *Blumea balsamifera* L., *Mormadica charantia* L.- Makiling v., and *Lagerstroemia specious* L. may be adulterated under 21 U.S.C. 342(f)(1)(B) as a dietary supplement that contains one or more new dietary ingredients at levels for which there is inadequate information to provide reasonable assurance that they will not present a significant or unreasonable risk of illness or injury. Adulterated or unsafe dietary supplements are prohibited under 21 U.S.C. 331(a) and (v) from being introduced or delivered for introduction into interstate commerce.

Your notifications will be kept confidential for 90 days after the filing date of February 11, 2002. After May 11, 2002, the four notifications will be placed on public display at FDA's Docket Management Branch in docket number 95S-0316. However, any trade secret or otherwise confidential commercial information in the notifications will not be disclosed to the public.

Prior to May 11, 2002, you may wish to identify in writing specifically what information in your notifications you believe is proprietary for FDA's consideration. Nevertheless, our Center's Freedom of Information Officer has the authority to make the final decision about what information in the notifications should be redacted before they are posted at Dockets.

If you have any questions concerning this matter, please contact us at (301) 436-2371.

Sincerely yours,

Felicia B. Satchell

Felicia B. Satchell
Director
Division of Standards
and Labeling Regulations
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition

KELATRON CORPORATION
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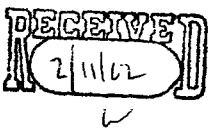

Mr. Gary Coody
Office of Nutritional Products
Labeling and Dietary Supplements (HFS-805)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, Md. 20740

Dear Mr. Coody,

In reference to the submission of information on the botanicals trademarked **Biodiamed, Biodiamend Biorenal and Biovitabronch/Biovitaflu** in accordance with the regulation:
TITLE: 21 Food And Drugs
Chapter I – Food and Drug Administration
Dept of Health and Human Services
Part 190 – Dietary Supplements
Subpart B—New Dietary ingredient Notification
Sec. 190.6 Requirement for premarket notification

Please accept the enclosed modified pages which include *Directions* (for use) under the *Condition of use* clause.
Also enclosed are additional materials (clinical trial data)on Biorenal for your review. I believe this was the missing information.

Please call me directly at my office in North Carolina, 252-234-7160 if further information is needed.

Thank you,

Mary Ann Coral-Amasifuen

From:
Mary Ann Coral-Amasifuen
Kelatron Corporation World Headquarters
1675 West 2750 South
Ogden, Utah 8440
Phone (801) 394-4558

Kelatron Corporation Botanical Division
2145 Barefoot Park, SW
Wilson, North Carolina 27893
Phone: (252) 234-7160

To:
Office of Nutritional Products
Labeling and Dietary Supplements (HFS-805)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, Md. 20740
Atten: Gary Coody

In accordance with:
TITLE: 21 Food And Drugs
Chapter I – Food and Drug Administration
Dept of Health and Human Services
Part 190 – Dietary Supplements
Subpart B—New Dietary ingredient Notification
Sec. 190.6 Requirement for premarket notification

(1) **Name and address of distributor**: Kelatron Corporation
1675 West 2750 South
Ogden, Utah 84401

(2) **Name of new dietary ingredient:** BioVitaflu / BioVitabronch (*Vitex negundo*, L)

(3) **Description of new ingredient:** BioVitaflu / BioVitabronch is the bulk pure leaf powder of the plant variety *Vitex negundo*, L. harvested for medicinal purposes in the Philippines. There has been clinical research done on the effectiveness of this plant for enhancing air flow in and out of lungs and reducing phlegm caused by congestion in the lungs. It is currently in use in the Asian market under the name Lagundi, which is the local name for the plant in southeast Asia.

(3) (i) **Level of new ingredient**: The product contains only the pure plant leaf powder of *Vitex negundo*, L and no other substance, to be sold in bulk powder form to retail manufacturers.

(3) (ii) **Condition of use**: : In general, to be used by adults (18 and over). Not to be used by lactating or pregnant women. Directions: One 600 mg capsule three times per day

(4) **History of use** *see attachment 4A*

(5) **Signature** _____ **Date** 2-5-02

January 18, 2002

MR. Coody,

I have made corrections to the Conditions of use portion in three of the applications.

We will send the full text article and remaining Condition of use modification when I arrive back to my office in North Carolina.

It would be helpful if you would log in the botanical products that are in Compliance with the information requested.

Thank you,

Mary Ann Cook-Gonsalves

From:
Mary Ann Coral-Amasifuen
Kelatron Corporation World Headquarters
1675 West 2750 South
Ogden, Utah 8440
Phone (801) 394-4558

Kelatron Corporation Botanical Division
2145 Barefoot Park, SW
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To:
Office of Nutritional Products
Labeling and Dietary Supplements (HFS-805)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, Md. 20740
Atten: Gary Coody

In accordance with:
TITLE: 21 Food And Drugs
Chapter I – Food and Drug Administration
Dept of Health and Human Services
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(1) **Name and address of distributor**: Kelatron Corporation
1675 West 2750 South
Ogden, Utah 84401

(2) **Name of new dietary ingredient:** BioVitaflu / BioVitabronch (*Vitex negundo*, L)

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(3) (i) **Level of new ingredient**: The product contains only the pure plant leaf powder of *Vitex negundo*, L and no other substance, to be sold in bulk powder form to retail manufacturers.

(3) (ii) **Condition of use**: : In general, to be used by adults (18 and over). Not to be used by lactating or pregnant women.

(4) **History of use**: *see attachment 4A*

(5) **Signature** _____ **Date** 1-18-02

addendum
(note: some duplicated

From:
Mary Ann Coral-Amasifuen
Kelatron Corporation World Headquarters
1675 West 2750 South
Ogden, Utah 84401
Phone (801) 394-4558

Kelatron Corporation Botanical Division
2145 Barefoot Park, SW
Wilson, North Carolina 27893
Phone: (252) 234-7160

To:
Office of Nutritional Products
Labeling and Dietary Supplements (HFS-820)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street SW
Washington, DC 20204

In accordance with:
TITLE: 21 Food And Drugs
Chapter I – Food and Drug Administration
Dept of Health and Human Services
Part 190 – Dietary Supplements
Subpart B—New Dietary ingredient Notification
Sec. 190.6 Requirement for premarket notification

(1) **Name and address of distributor**: Kelatron Corporation
1675 West 2750 South
Ogden, Utah 84401

(2) **Name of new dietary ingredient:** BioVitaflu / BioVitabronch (*Vitex negundo*, L)

(3) **Description of new ingredient:** BioVitaflu / BioVitabronch is the bulk pure leaf powder of the plant variety *Vitex negundo,* L. harvested for medicinal purposes in the Philippines. There has been clinical research done on the effectiveness of this plant for enhancing air flow in and out of lungs and reducing phlegm caused by congestion in the lungs. It is currently in use in the Asian market under the name Lagundi, which is the local name for the plant in southeast Asia.

(3) (i) **Level of new ingredient**: The product contains only the pure plant leaf powder of *Vitex negundo*, L and no other substance, to be sold in bulk powder form to retail manufacturers.

(3) (ii) **Condition of use**: Clinical trials indicated that BioVitaflu/BioVitabronch may be effective in relaxing smooth muscle tissue and ease night time coughing.

(4) **History of use**: *see attachment 4A*

(5) **Signature** Mary Ann Coral **Date** 1·10·02

LAGUNDI

(*Vitex negundo* L.)

ORIGINAL ARTICLE:

THE EFFECT OF "LAGUNDI" (a local herb) TABLETS ON BRONCHIAL ASTHMA IN ADULTS: RANDOMIZED DOUBLE BLIND STUDY WITH THEOPHYLLINE*

By: Romeo P. Chu, M.D.**

ABSTRACT

Forty otherwise healthy asthmatics were included in a randomized double blind comparative study between lagundi tablets and the standard drug theophylline. There were 20 subjects per treatment group; 7 of the subjects were males and 33 females. The patient profile of both treatment groups were comparable. Likewise, the baseline parameters of both groups were also comparable. Results showed that both lagundi and theophylline caused significant bronchodilation over time. Statistical analysis showed significant increase in the mean peak expiratory flow rate (PEFR) of the lagundi group beginning at the 3rd hour. This shows the onset of action of lagundi to be at 3 hours postdosing. For the theophylline group, significant increase in the PEFR values was noted at 1 hour which corresponds to its onset of action. ANOVA with repeated measures showed no significant difference between lagundi and theophylline with respect to their effects on PEFR. However, since the sample size is inadequate, it cannot yet be concluded that lagundi is as effective as theophylline. Patients treated with lagundi failed to show a significant improvement of their wheezing over time but might have prevented the wheezing from getting worse. Patients treated with theophylline however showed significant improvement of their wheezing as early as the second hour. The theophylline treated patients had significantly better wheezing scores than the lagundi group at the 6th, 8th, 24th and 48th hour. There were no significant difference in the severity of cough, dyspnea and chest pain in both treatment groups over time. However, the theophylline treated group had better "cough" than the "lagundi" group at the 24th and the 48th hour. The theophylline group had also better "dyspnea" scores than the lagundi group at the 48th hour. There was no significant difference between lagundi and theophylline in terms of the effects on pulse rate, respiratory rate and blood pressure (BP) readings. However, there was significant decrease in the mean sitting systolic BP and standing diastolic BP over time. This needs further investigation. Side effects reported in the lagundi group were vomiting, desquamation of the skin over the palms and increased frequency of urination. In the theophylline group, the side effects reported were nausea, vomiting, cold sweats, palpitations, tremors, headache and epigastric pain. Overall, lagundi displayed significant bronchodilating effects. Although theophylline has a slight edge in terms of therapeutic efficacy, lagundi still holds to be a promising drug in the future.

INTRODUCTION

The use of plants for medicinal purposes is as old as man himself. Primitive man probably learned their medicinal value from intuition and observation of the animals around him. Through trial and error, he discovered the efficacy of certain plants for certain ailments and he passed this knowledge on to his neighbors. From such beginnings sprung our present knowledge of the use of plant constituents in the treatment of disease.

Philippine flora abounds with plants of medicinal value. Scientific proof of efficacy, established through the isolation of their active

* *FIRST PRIZE winner, 6th PAFP-SANDOZ RESEARCH CONTEST, Feb. 19, 1988, Manue Midtown hotel*

** *Resident Physician, Dept. of Family Medicine (1985-87), Philippine General Hospital, Manila, Philippines*

constituents and studies on their pharmacologic actions, has been accomplished on some of these plants. This work was done principally by the University of the Philippines, the National Institute of Science and Technology (NIST) and the Philippine Council for Health Research and Development (PCHRD). However, there remains a large number of plants, widely used in folk medicine, still to be investigated. One of these plants is Lagundi.

Vitex negundo (Lagundi, Tag.) is an erect, branched shrub which grows throughout the Philippines. It is found more commonly in low and medium altitudes and in waste places, thickets, and similar locations. The leaves usually have 5 leaflets (rarely 3) which are palmately arranged. These leaves are found to have an essential oil and resin, while the fruit contains an acid resin and an astringent organic acid. The leaves and seed of the plant were first reported as a medicine by Fr. Clain. Thereafter, more medicinal uses for the plant have been reported, among which are: as cleanser for ulcers, as lactagogue, febrifuge, expectorant, wound disinfectant and for flatulence. The leaves in particular have been used as insecticide, anti-inflammatory, expectorant, and for catarrh and headache.

Open clinical trials have shown that the decoction of leaves of lagundi decreased the frequency of cough and increased the volume of expectoration. In a study in guinea pigs, using citric acid as cough inducer, the antitussive effect of the decoction was comparable to that of dextrometorphan.

Anecdotal reports seem to show a favorable response of asthmatic patients to lagundi leaves decoction. The bronchodilating activity of lagundi leaves has repeatedly been shown using the cat tracheal chain model. One child in acute asthma showed improvement of FEVI, FVC and PEFR after a single dose of lagundi leaves decoction.

OBJECTIVES:

1. To determine the therapeutic efficacy of lagundi tablets on bronchial asthma in adults.
2. To compare the effect of lagundi tablet to that of theophylline tablet on bronchial asthma.
3. To determine the onset of action of the bronchodilating activity of lagundi tablet on bronchial asthma.
4. To compare the adverse effect/s of lagundi tablets (if any) to that of theophylline tablets on bronchial asthma.

METHODOLOGY:

A. Preparation of Test Drugs

1. Lagundi tablets made from pulverized dried lagundi leaves were manufactured by PCHRD. The tablets utilized were from lot no. 28108601.
2. Theophylline tablets (125 mg/tab) were street purchased.

B. Selection of Patients

1. Inclusion criteria:

a. Males and females 14 years and above with definite history of asthma.

b. Patients whose PEFR is less than 85% of predicted value and who are able to demonstrate that their bronchospasms is reversible in the following manner:

The patient's peak expiratory flow rate is recorded before and 15 minutes after 2 inhalations of a metered dose (100 mcg) of salbutamol aerosol. Only patients whose PEFR is increased by 20% will be admitted to the study.

c. Except for asthma, patients must be in good general health.

d. Patients who have been fully informed of the possible risks and benefits of participation and have voluntarily agreed to participate in this study. For minors, parents or guardians who are fully informed shall also sign the consent.

2. Exclusion criteria:

a. Patients with severe asthma as defined:
1. grade 2A or worse (see Appendix A)
2. presence of resting tachycardia
3. pulsus paradoxus k 20 mmHg
4. PEFR 120 or less
5. impending ventilatory failure

b. Patients who require maintenance doses of any medications other than the test drug. Patients on beta – 2 agonist agents and short or long acting theophylline preparations are required to stop medications at least 24 hours prior to the study.

c. Patients who have used systemic steroids chronically within six months before entry into the study; or have used a single dose of dexamethasone or betamethasone within six weeks before entry into the study; or have used systemic short acting steroids within 14 days before entry into the study.

d. Patients who have used disodium cromoglycate or ketotifen within seven days before entry into the study.

e. Patients with any of the following:

1. cardiac arrhythmia
2. moderate to severe hypertension
3. patients on beta blocker therapy
4. insulin dependent diabetes mellitus
5. significant hepatic or renal disease

f. Patients who are pregnant or lactating.

C. Study Design

This is a double blind standard drug controlled study utilizing 40 patients who are randomly assigned to 2 groups: Group 1 (20 patients) to receive theophylline (3 mg./kg./dose) repeated every 8 hours for 9 doses. Group 2 (20 patients) to receive lagundi (15 mg./kg./dose) repeated every 8 hours for 9 doses.

After a patient has been selected as a candidate for the study and has given informed consent, the following procedures were performed.

1. complete medical history and physical examination with emphasis on PEFR, sitting and standing blood pressure, respiratory rate, pulse rate and auscultation of the chest.

2. routine laboratory tests:

a. hematology: hemoglobin, hematocrit, total white cell count, differential count, erythrocyte sedimentation rate, reticulocyte count and platelet count.

b. blood chemistries: BUN, creatinine, SGPT, RES

c. urinalysis

3 chest x-ray (optional)

In all patients enrolled into the study, sufficient time was allowed for recovery from the salbutamol test (at least 8 hours). Once the PEFR is again less than 85%, then the study is resumed.

During the course of the study, all food substances must be caffeine-free. No coffee, tea, chocolate or softdrinks were allowed.

Prior to giving of medications (baseline) and at 15 minutes, 30 minutes 1, 2, 3, 4, 6, 8, 24, 48 and 72 hours post-dosing, the following were examined (or asked) and properly recorded:

1. sitting and standing blood pressure
2. pulse rate
3. respiratory rate
4. PEFR at standing position (the highest of at least 3 acceptable efforts was recorded)

5. chest auscultation noting the degree of wheezing scored as follows: none – 0; mild -1; moderate – 2; severe – 3.
6. severity of cough scored as above
7. degree of dyspnea scored as above
8. degree of chest pain scored as above

Side effects or adverse reactions were described and properly recorded.

D. Intercurrent Events

Patients were not allowed to take concomitant medications during the study. If the patient does not respond to either lagundi or theophylline, then salbutamol tablets at a maximum dose of 2 mg. every 8 hours will be added to the regimen and recorded.

DATA ANALYSIS

Analysis of variance (ANOVA) with repeated observations with respect to time was used for data on theophylline and lagundi doses for the four variables: blood pressure, pulse rate, respiratory rate and PEFR. If a statistically significant result is obtained, Duncan Multiple Range Test was employed to determine the specific periods of observation which are significantly different from baseline.

Friedman two way analysis of variance was employed to determine if there was significant difference in the severity of cough, wheezing, dyspnea and chest pain over time.

Mann-Whitney U Test was used to determine if there was significant difference between the two treatment groups with respect to their effect on the severity of wheezing, cough, dyspnea and chest pain.

RESULTS AND DISCUSSION

From Sept. 22 to Dec. 31, 1987, 43 subjects participated in the clinical trial. 3 dropped out of the study after 24 hours. All of them were in the theophylline group. The first one dropped out to take care of her sick child; the second due to inclement weather (typhoon) and the third for unknown reason. Only 40 subjects were included in the following discussion.

Patient Profile

The 40 subjects were equally distributed for each treatment group – 20 in the lagundi group and 20 in the theophylline group. There were 7 males and 33 females with a ratio of 1:4.7. In the lagundi group, there were 19 females and only 1 male while in the theophylline group, there were 14 females and 6 males.

The mean age for the lagundi group (31.2 years) was slightly lower than the theophylline group (34.7 years). The mean age for all subjects was 32.95 years. The age range for the lagundi group was from 20 to 48 years while that of the theophylline group was from 16 to 72 years. Mean duration of illness for the lagundi group was 13.3 years while that of the theophylline group was 18.1 years. The mean duration of illness for all subjects was 15.7 years. The frequency of attacks was similar for both groups which ranged from weekly to yearly. All the subjects included in the study had previously been taking either a theophylline preparation, beta-2 agonist agents, or both. There were 3 subjects with concomittant illness. 2 patients in the lagundi group had mild hypertension and 1 patient in the theophylline group had nodular non-toxic goiter.

Laboratory Tests Results

All blood chemistries were within normal limits except for 2 patients. One of these is in the lagundi group and has a WBC count of 13,000/mm3. The other patient is in the theophylline group and has a WBC count of 10,000/mm3. Both have normal differential counts and had no clinical evidence of infection.

2 patients in the lagundi group has slightly elevated eosinophil count at 0.04 x 109/L. 2 patients in the theophylline group also showed elevations at 0.03 and 0.07 x 109/1 respectively.

25 out of the 40 subjects had their chest x-ray done within the year. All showed normal findings except for 4 patients. 2 patients showed minimal infiltrates in the upper lung fields interpreted as minimal pulmonary tuberculosis activity undetermined, one of these belong to the lagundi group while the other was in the theophylline group. One of the patients in the lagundi group had a chest x-ray which showed emphysematous changes while the other patient in the theophylline group showed streaky densities on both lower lung fields interpreted as chronic non-specific inflammatory disease.

Figure 1 illustrates graphically the mean PEFR values of both the lagundi and theophylline treated groups over time.

The analysis of variance (ANOVA) with repeated measures showed a significant difference in the mean PEFR values of both treatment groups over time. This means that both drugs, lagundi and theophylline, caused significant bronchodilation over time. Duncan multiple range test showed significant increase in the mean PEFR values (from baseline fo 238.75 L/min.) of the lagundi group beginning at the

third hour reaching 257.5 L/min. (This was sustained up to 8 hours). This means that the onset of action of lagundi is at 3 hours post-dosing. For the theophylline group, significant increase in the PEFR value was noted at 1 hour (from a baseline of 257.75 L/min. to 288.75 L/min.) which corresponds to its onset of action. This effect was sustained throughout the study period.

Comparing the 2 drugs in terms of their effect on the PEFR values using the ANOVA with repeated measures, the results showed no significant difference between the two treatment groups at $P > 0.05$. However, since the sample size is still inadequate, it cannot yet be concluded that lagundi is as effective as theophylline.

Figure 2 illustrates graphically the mean pulse rate of both treatment groups over time. ANOVA with repeated measures showed no significant difference in the pulse rate of both treatment groups over time. This means that both drugs are safe in that they do not significantly affect the pulse rate. They are neither myocardial stimulants nor depressants.

There was also no significant difference between the two drugs in terms of their effect on the pulse rate.

Figure 3 illustrates graphically the mean respiratory rate (RR) of both treatment groups over time. The ANOVA showed no significant difference in the mean RR of both treatment groups over time. This could be so because most patients included in this study had only mild asthma and are thus not tachypneic. In fact, the mean RR for all subjects was only 20.5/min. Even if the patients responded to the medications and had relief of their bronchospasm, no significant drop in the RR is expected because of the above stated reason. What is important to note is that the mean RR did not increase which means that the patients did not get worse.

Figure 4 illustrates graphically the mean sitting blood pressure (BP) of both treatment groups over time. There was significant difference in the mean sitting systolic BP over time for both treatment groups. In the lagundi group, the mean baseline systolic BP at sitting position was 109.75 mmHg. At 30 mins. and at the 6th hour, this was significantly lower at 30 mins. with a mean reading of 106.9 mmHg. This was also noted at the following observation periods: 2 hours (hrs.), 4 hrs., 5 hrs., 6 hrs., 8 hrs. and 72 hrs. These changes could be due to the relief of bronchospasms or due to the fact that the patients were rested for a longer period of time. It is also important to note that although there was a significant decrease in the sitting systolic BP, this effect was not consistent throughout the study periods. No patient reached hypotensive levels nor were there complaints of dizziness attributable to the decline in BP. All these plus the fact that all patients (except for the 2 previously mentioned hypertensives) were normotensive seem to point out that these differences were not really that important. These findings were also not consistent in the 2 patients (both in the lagundi group) with mild hypertension. One patient had a slight increase in systolic BP while the other had a slight decrease.

Comparing the two, there was no significant difference between lagundi and theophylline in terms of their effect on sitting systolic BP.

For the sitting diastolic BP, there was no significant difference in both treatment groups over time. There was also no significant difference between the two groups in terms of their effect on sitting diastolic BP.

Figure 5 illustrates graphically the mean standing BP readings of both treatment groups over time.

ANOVA with repeated measures showed no significant difference in standing systolic BP readings of both treatment groups over time. There was also no significant difference between the two drugs in terms of their effect on standing systolic BP.

There was a significant decrease in the mean standing diastolic BP for both treatment groups over time. For the lagundi group, the baseline mean diastolic BP in standing position was 84 mmHg and there was a significant decrease to 77 mmHg noted at the 4th hour up to the 8th hour and at the 24th hour. For the theophylline group, the baseline mean standing diastolic BP was 79.8mmHg which significantly decreased to 75 mmHg at 30 mins., the 1st hour and the 4th hour. Again, the reasons previously cited could be used to explain the significant decrease in BP readings, i.e. – relief of bronchospasm and longer period of rest. Similarly,

the significant decrease was not persistent throughout the study period and that the patients did not reach hypotensive levels.

Chest Findings

The study shows that in the severity score for wheezing in the lagundi group over time, the higher the rank sum, the more severe is the wheezing. Note that the changes in the scores are minimal. Using the Friedman 2 way ANOVA, there is no significant difference in the severity of wheezing at $P > 0.05$. This means that patients treated with lagundi failed to show a significant improvement of their wheezing over time but might also mean that lagundi prevented their wheezing from getting worse.

The severity scores for wheezing in the theophylline group over time showed results of statistical analysis indicating significant improvement in the severity of wheezing at $P > 0.05$. This was noted as early as the second hour and was sustained throughout the study period.

Mann Whitney U test was utilized to compare the two treatment group with respect to their effects on wheezing. There was a significant difference between the lagundi and theophylline treated group at the 6th hour, 8th hour, 24th hour and 48th hour. This means that the improvement in the severity of wheezing in the theophylline treated group was significantly better than the lagundi group at the observation period stated above.

Cough

Statistical Analysis of the severity scores for cough in the lagundi group over time showed no significant difference in the severity of cough in this treatment group at $P > 0.05$. This means that patients treated with lagundi failed to show significant improvement or deterioration of their cough over time. A larger sample size might be able to detect a significant difference. Although previous studies showed lagundi to be effective against cough of viral origin, the parameters used was more of frequency rather than severity, so the results are not quite comparable.

Statistical analysis of the severity scores for cough in the theophylline treated group over time also showed no significant difference in the severity of cough in this treatment group over time at $p > 0.05$. Although theophylline afforded significant relief of bronchospasm and improvement of wheezing, there is still no significant improvement of its associated cough. A larger sample size might be able to detect a significant difference.

Comparing the two treatment group with respect to their effect on cough, there is a statistically significant difference between the lagundi group and the theophylline group at the 24th and 48th hour. This means that the improvement in the severity of cough in the theophylline treated group was significantly better than the lagundi treated group at the above stated observation periods.

Dyspnea

Statistical analysis of the severity scores for dyspnea in the lagundi treated group over time showed no significant difference in the severity of dyspnea in this treatment group over time at $p > 0.05$. This means that although patients treated with lagundi had significant relief of their bronchospasm, yet there was no significant improvement in the severity of their dyspnea. However, lagundi might have protected them from getting worse.

With regards the severity scores of dyspnea in the theophylline treated group over time, statistical analysis showed no significant difference in the severity of dyspnea in this treatment group over time at $p > 0.05$. This means that the degree of dyspnea in patients treated with theophylline neither improved nor worsened.

Comparing the two treatment groups with respect to their effect on dyspnea, there was a statistically significant difference between the lagundi group and the theophylline group at the 48th hour. This means that the improvement in the severity of cough in the theophylline treated group was significantly better than the lagundi treated group at the observation period stated above.

Chest Pains

Friedman 2 way ANOVA showed no significant difference in the severity of chest pains over time for the lagundi group at $p > 0.05$. This means that patietns treated with lagundi failed to show a significant improvement or worsening of their chest pain over time.

For the severity scores for chest pain in the theophylline group over time, statistical analysis showed no significant difference in the severity of chest pains over time for this treatment group at $p > 0.05$. This means that patients treated with theophylline failed to show a significant improvement or worsening of their chest pain over time.

Comparing the two treatment groups with respect to their effect on chest pains, there is no significant difference between the lagundi group and that of the theophylline group at any observation period. No t one drug is superior to the other with respect to their effect on chest pain.

Number of Salbutamol Tablets

Twelve patiens (30% of the sample size) took salbutamol tablets after 24 hours because they developed asthmatic attacks. Eight (8) were in the lagundi group and four (4) in the theophylline group. Of the 8 subjects in the lagundi group, 1 patient took 8 Salbutamol tablets (This patient had been on prednisone for 10 days but has stopped since 3 weeks prior to the study and had fair control of her asthma. He bronchial airway hyper-reactivity might have flared up again); 1 patient took 4 tablets; another patient took 2 tablets and 3 patients took 1 tablet each. The total number of salbutamol tablets taken in the lagundi group was 27. Of the 4 patients in the thophyllinine group, 1 patient took 3 tablets and 3 patients took 1 tablet teach. Total number of salbutamol tablets taken in the theophylline group was only 6. No statistical analysis was employed to analyze the difference between the two treatment groups in terms of the number of additional medications taken but it seems apparent that theophylline patients fared better than the lagundi patients in that they took less salbutamol tablets.

The fact that these patients took salbutamol tablets did not invalidate the previous conclusions drawn for the above parameters, regardless of the treatment groups. All patients took these additional medications after the first 8 hour observation period which leaves us to account only for the 24th, 48th and 72nd hour. Reviewing the individaul charts however showed that all parameters went down (reflecting worsening condition) during these three observation periods even if the patients took salbutamol tablets in contrast to the general trend which shows that the parameters were going up (reflecting improving condition). This means that the intake of salbutamol tablets did not contribute significantly enough to alter the results of the different parameters under study.

Adverse Effects

Two (2) patients in the lagundi group complained of vomiting; another 2 noted desquamation of the skin over their palms and another one complained of increase frequency (but not amount) in urination.

Three (3) patients in the theophylline group complained of nausea and one of them vomitted; 2 complained of cold sweats and palpitations; another 2 complained of headaches; 1 complained of epigastric pain and another one complained of dizziness.

CONCLUSION AND RECOMMENDATIONS

Results of this study showed that lagundi caused significant bronchodilating activity and had fewer side effects. Although theophylline has a slight edge in terms of therapeutic efficacy, yet lagundi still holds to be a promising drug in the future. The lagundi tablets used were but made from crude dried leaves and might contain only minimal active compounds. Thus, the dosage used although at 15 mg/kg./dose might actually be inadequate. Further investigations must be undertaken and the following steps are recommended.

1. Active principle should be isolated.
2. Studies should be done correlating bronchodilation with serum levels.
3. Pharmacokinetics and pharmacodynamics of lagundi should be studied.

The increasing uses of medicinal plants, the present return to Mother Earth and nature's product, the number of people from all over the world who rely partly or completely on herbal cures and the success they achieve, are clear indications of the position these plants occupy in the practice of medicine today.

In our country, the cost of imported medicine is becoming prohibitive. This shows us clearly the urgent need for extensive research on our medicinal plants. Never before had we been so forced to rely upon our own resources as we are then when the very life of our nation (for people are the nation) depended upon the herbs that God had graciously given us.

LAGUNDI IS A SPARK AND WE HOPE THIS SPARK SHALL START A FLAME.

Appendix A

Grading of Asthma

Grade 1A

Patient only able to carry housework or job with great difficulty. Sleep frequently disturbed.

Grade 1B

Patient only able to carry housework or job with great difficulty. Sleep frequenty disturbed.

Grade 2A

Patient confined to chair or bed but able to get up with moderate difficulty. Sleep is disturbed with little or no relief from inhaler.

Grade 2B

Patient confined to chair or bed and only able to get up with great difficulty. Unable to sleep. Pulse rate over 120 per minute.

Grade 3

Patient totally confined to chair or bed. No sleep. No relief from inhaler. Pulse rate over 120 per minute.

Grade 4

Patient immobilized and completely exhausted.

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Alice Caragay, M.D.
Maria Teresa Angeles, M.D.
Jimmy Chua, M.D.
Industrial Pharmacology, U.P., Manila
NSTA – Project 7711
PCHRD

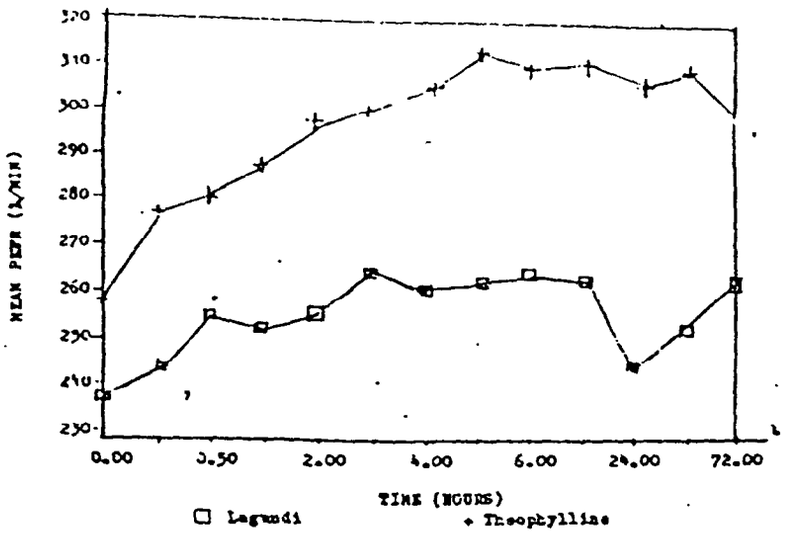

FIG. 1. MEAN PEFR VALUES OF LAGUNDI AND THEOPHYLLINE TREATED GROUPS OVER TIME

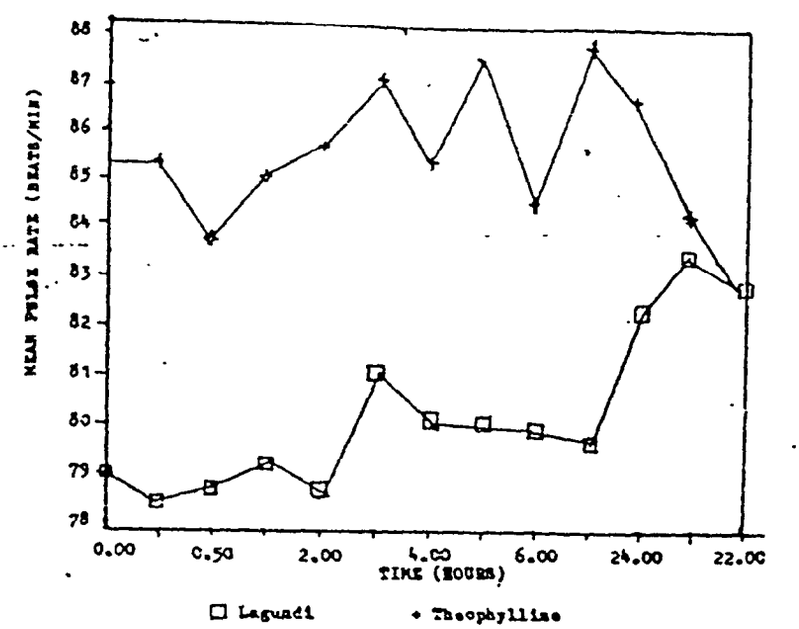

FIG. 2. MEAN PULSE RATE OF LAGUNDI AND THEOPHYLLINE TREATED GROUPS OVER TIME

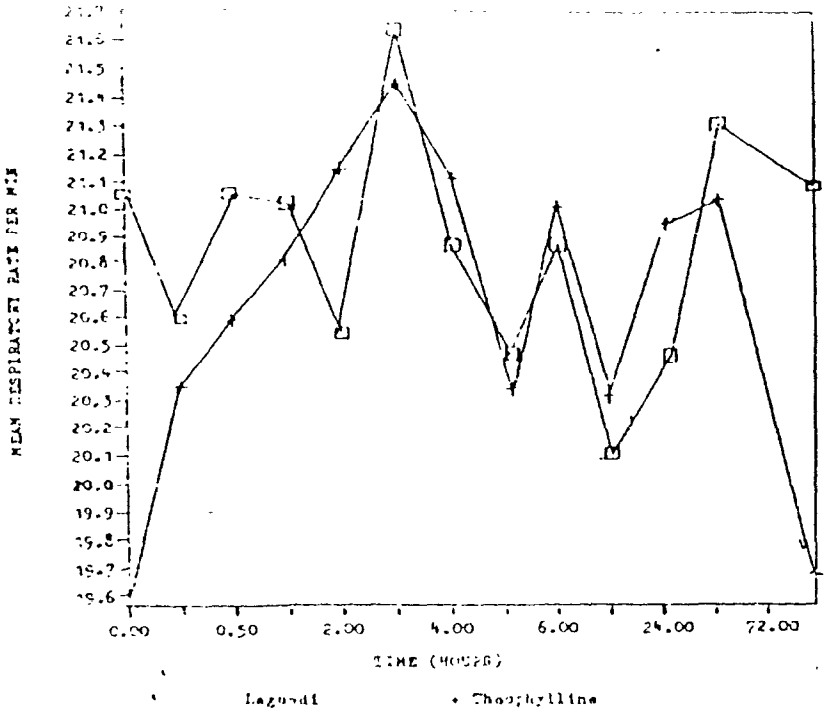

FIG. 3. MEAN RESPIRATORY RATE OF LAGUNDI AND THEOPHYLLINE GROUPS OVER TIME

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SUBMITTED CLINICAL STUDY
REDACTED IN ITS ENTIRETY
CONTAINS
CONFIDENTIAL COMMERICAL INFORMATION

Copy Vitex negundo L. - BioVitaflu/Biovitabronch

From:
Mary Ann Coral-Amasifuen
Kelatron Corporation World Headquarters
1675 West 2750 South
Ogden, Utah 8440 |
Phone (801) 394-4558

Kelatron Corporation Botanical Division
2145 Barefoot Park, SW
Wilson, North Carolina 27893
Phone: (252) 234-7160

To:
Office of Nutritional Products
Labeling and Dietary Supplements (HFS-820)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street SW
Washington, DC 20204

In accordance with:
TITLE: 21 Food And Drugs
Chapter I – Food and Drug Administration
Dept of Health and Human Services
Part 190 – Dietary Supplements
Subpart B—New Dietary ingredient Notification
Sec. 190.6 Requirement for premarket notification

(1) **Name and address of distributor**: Kelatron Corporation
1675 West 2750 South
Ogden, Utah 84401

(2) **Name of new dietary ingredient:** BioVitaflu / BioVitabronch (*Vitex negundo*, L)

(3) **Description of new ingredient:** BioVitaflu / BioVitabronch is the bulk pure leaf powder of the plant variety *Vitex negundo,* L. harvested for medicinal purposes in the Philippines. There has been clinical research done on the effectiveness of this plant for enhancing air flow in and out of lungs and reducing phlegm caused by congestion in the lungs. It is currently in use in the Asian market under the name Lagundi, which is the local name for the plant in southeast Asia.

(3) (i) **Level of new ingredient**: The product contains only the pure plant leaf powder of *Vitex negundo*, L and no other substance, to be sold in bulk powder form to retail manufacturers.

(3) (ii) **Condition of use**: Clinical trials indicated that BioVitaflu/BioVitabronch may be effective in relaxing smooth muscle tissue and ease night time coughing.

(4) **History of use**: *see attachment 4A*

(5) **Signature** _____ **Date** 12-10-01

RECEIVED 1/3/02

ATTACH 4A

REPUBLIC OF THE PHILIPPINES
DEPARTMENT OF HEALTH
BUREAU OF FOOD AND DRUGS
Alabang, Muntinlupa
Metro Manila

Nº 29690

P.S.D. Form No. 1
Registration Status :
BFAD Registration No. : HDL-36
Classification Otc-initial

CERTIFICATE OF PRODUCT REGISTRATION

Pursuant to the provisions of Republic Act No. 3720 as amended, known as the Foods, Drugs and Devices and Cosmetics Act, and consistent with R.A. 6675, known as the Generic Act of 1988, the product more particularly described hereunder has been found to conform with requirements and standards for registration of pharmaceutical products per A.O. No. 67 s. 1989.

Name of Products : Generic : LAGUNDI 600 mg TABLET
Vitex negundo L. (Fam. Verbenaceae)

Brand (if any) : ASCOF FORTE 600 mg TABLET

Manufacturer / Trader : Pascual Laboratories Inc.
Balagtas, Bulacan

Approved Indication (s) : For the treatment of bronchospasm in acute bronchial asthma, chronic bronchitis and other broncho pulmonary disorders.

Claimed Stability : 24 months

This registration shall be valid for five year(s) and shall expire on Sept. 09, 2003 subject to the following conditions:

CERTIFIED TRUE COPY:
JONATHAN P. ROMAGOS
Special Authenticating Officer
BUREAU OF FOOD AND DRUGS
Date: 9-22-98
VALID WITHOUT OFFICIAL SEAL

No change in the formulation, labelling and commercial presentation of this product shall be made during the effectivity of this registration without the approval of this Office.

This registration is subject to suspension, cancellatoin or recall should violation of any provision of R.A. 3720, as amended, and/or regulations issued thereunder involving the product be committed.

Witness My Hand and Seal of this Office, this 09th day of September, 1998

SL (Cellofoil)
P6,420
9975454
97A-305/GIM/cora

QUINTIN L. KINTANAR, M.D., Ph. D.
Director - CESO I

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PR...
Continued from page 11

. Romulo, and gave it to
ıe.

I thanked him profusely
or the nice breakfast and
icture commenting: "Sir,
ou wrote here on your
icture Ambassador Rodolfo
.rizala. I am not an
.mbassador but a
ounselor." CPR said: "I
now, but you will be an
.mbassador soon. Go now
ecause I have the new US
.mbassador for breakfast
oday. Happy trip and good
ıck!"

As I went out to the
arking lot to get my old
ilapidated Volkswagen, I
ıw the big, black and shiny
mousine of the U.S.
.mbassador entered the
ıain gate with the American
ag fluttering in the early
ıorning breeze at its right
:nder. I wondered how
ıany breakfasts CPR hosted
t his "Kasiyahan" residence
ıat morning.

Shortly after I established a
:sident embassy in Santiago,
:hile, Gen. Romulo had me
)pointed by the President as
rst Philippine resident
mbassador to Chile.

That was General CPR, the
:cretary of Foreign Affairs
ho served in various
ıpacities all Presidents of the
hilippines from Manuel L.
)uezon of the Philippine
:ommonwealth to Pres.
Iarcos of our 3rd Republic.
le gave equal importance to
is subordinates with that of
)reign diplomats by
ıviting them to breakfast at
is "Kasiyahan" residence
/henever he has important
:ssage or assignment to
ıake.

*Last December 15, 1997 was
he 12th Anniversary of the
eath of Secretary of Foreign
ffairs Carlos P. Romulo)* ●

Lagundi: The Miracle Medicinal Plant

By Vicenta Mendoza Escobar

THE medicinal plant *Lagundi* is very much in the news. People are now talking about *Lagundi* – a medicinal plant with amazing multi-cure power that has already been approved by our Bureau of Food and Drug Administration.

Lagundi is effective in lowering fever of viral origin and for coughs and colds. So when one has the flu, colds, measles, chicken pox, or mumps, — all one has to do is to take one stem of *Lagundi* (which contains five leaves for every cup of water) and boil the *Lagundi*. Unbelievably, *Lagundi* is safe and is effective as any of the pharmaceutical antipyretic in the market today.

We are currently spending some P1 Billion a year for anti-fever medicine out of our total P30 Billion expenditure for pharmaceuticals. We also spend some P3 Billion a year for cough syrups. The good news is that studies have shown that *Lagundi* is just as effective as the popular cough syrups in the market today.

Clinical trials have also indicated that *Lagundi* is effective for bronchial asthma. It has anti-histamine and bronchial relaxing as well as mild antimicrobial activities.

Studies conducted by Dr. Victoria Masilungan presented to the Graduate School of Centro Escolar University as early as 1963 showed that *Lagundi* has anticancer activity since it can control tumor growth in-vitro and in-vivo clinical studies.

Today, there is a growing worldwide interest in medicinal plants and traditional methods of healing. What is the reason for such interest? Mainly because the result of research

Leaves with flowers of *Lagundi* (Vitex negundo) - useful for fever of viral origin

...ave tremendously ...nced a growing ...ersal of traditional perceptions.

It is now the consensus thinking that both the traditional methods of healing including the use of medicinal plants and the modern medicines work well – and their integration leads to better treatment.

Lagundi is just as effective as the popular cough syrups in the market today.

The growing acceptance of medicinal plants these days can be attributed to the disappointment of modern man in most synthetic "miracle drugs" that have caused unexpected and sometimes terrifying side effects.

It is reported that the incidence of complications in drug therapy in the United States is about 10% and that approximately 5% of patients admitted to their general hospitals suffer not from diseases but from serious drug reactions.

The growing concern over the harmful side-effects of some drugs if improperly taken have encouraged people to go back to the use of medicinal plants especially in primary health care.

For instance, it is now acknowledged that the use of antibiotics for viral infections not only prolongs but also worsen viral infection. While before it was considered that a possible secondary infection can be prevented by prophylaxis treatment with antibiotics – this is now considered an obsolete modality of treatment.

While studies indicate that most viral infections are self-limiting and there as yet no drugs developed that can scientifically prevent colds or reduce their duration – many people still spend a lot for over-the-counter remedies for cough and colds unnecessarily exposing themselves to the risk of harmful side effects.

Fever is now considered - not as an illness itself but as a protective mechanism of the body that also serves as a warning symptom of an infection that needs to be properly treated.

The use of *Lagundi* as an antipyretic for fevers of viral origin has enormous potentials not only as an effective modality of treatment but also because the present market for antipyretics in the United States is about $3.2 Billion. If we can tap just 10% of that market, we can have a new source of livelihood for our rural areas.

Lagundi is a fast growing tree. It can provide income seven months after it is planted. Distributing *Lagundi* seedlings to our 45,000 *barangays* throughout the country is actually hastening our dream to plant one billion trees. Not to mention the livelihood opportunities and the availability of cheap anti-fever and cough medication critically needed in our primary health care program. ●

NORWAY...

Continued from page 7

On the home front, the approach of Christmas is signaled by the blended smells of exotic spices and goodies in the oven, which at Christmas means gingersnaps, doughnuts, cones and all the other traditional cakes and cookies which are a must for most people at Christmas: many families still call for the traditional "7 kinds."

Most families also stick to special Christmas dinner traditions. Along the coast, the main dish at home on Christmas Eve is often fresh cod or halibut or lutefisk, while in eastern Norway many prefer pork ribs with pork sausage patties and Christmas sausages. Dried mutton ribs are a west coast specialty. A popular meal earlier in the day, while the other preparations are in full swing, is rice porridge, and many families have rice cream with red fruit sauce for their Christmas dinner dessert.

In the cities and towns of today [illegible] to simplify the traditional celebrations. Even so, many of the time-honored traditions are still upheld.

The gifts are still opened on Christmas Eve and carols are still sung around the tree. The traditional foods, the porridge, the "lutefisk" or ordinary codfish, the various pork dishes and the "julekake," are still served; but the most complicated pork dishes have most probably been bought readymade, and there is a fair chance that the cakes will have come from a bakery.

However, the custom of paying visits to friends and relatives during the Holiday week is still kept up, and there is also a tradition of Christmas hospitality even to strangers, in keeping with the feeling that nobody ought to be alone and unhappy on Christmas Eve.

Moreover, the foreign visitor who knows what to look for will soon discover that there is still a distinct Norwegian flavor even in those busy preparations for the Holiday in the city streets.

There is, for one thing, the whiteness: not only the whiteness of the snow, but also the white lights used for decorations, so unlike the 7-colored ones used in many other countries. And there are the traditional Christmas dishes and small cakes, the straw decorations and the "nisse" dolls, all prominently displayed in the stores. He or she will also find that some of the shop window displays have typically Norwegian themes: the "nisse" sitting in the barn with his bowl of porridge, for instance, or the sheaf of oats full of gaily-colored birds.

There are also many things that may be seen in other places: the Santa Clauses in the large department stores with their beards and red costumes, the Christmas trees and decorations, the happy and expectant people.

Moreover, if the opportunity presents itself, a visitor to a Norwegian town at Christmas should give him or herself the treat of sampling the Christmas buffet of one of the well-known restaurants. ●

(By Vera Henriksen and Brita Drangsholt Jaksjo. Courtesy of the Royal Norwegian Embassy)

Manila Standard

EALTH&MEDICIN

Sunday, January 11, 1998

DoST promotes herbal medicines for asthma, kidney stones

When asthma attacks become more frequent or kidney stones get in the way of a healthy system, herbal medicine presents itself as an effective alternative medicine. As new studies reveal, certain herbs can readily provide the cures.

Lagundi and *Sambong* leaves, two of a wide variety of plants collected for research by the Department of Science and Technology (DoST), through the National Integrated Research Program on Medicinal Plants (NIRPROMP), were proven to heal patients with asthma and kidney stones, respectively.

Lagundi contains a smooth muscle relaxant and antihistamine, *Chrysophenol D*, clinically proven to relieve cough due to colds and flu. It is also known to ease mild to moderate brochospasm among children and adults with obstructive airway diseases like asthma and bronchitis.

Sambong, on the other hand, is highly recommended for patients with urinary tract stones. It effectively dissolves or decreases the size of kidney stones. It is also indicated as a diuretic in patients with mild to moderate congestive heart failure and edema. Moreover, it was found to be a potassium-sparing diuretic.

According to Dr. Pacita Zara, executive director of the DoST's Philippine Council for Health Research and Development (PCHRD), it took the DoST 20 years to validate these findings.

"At that time, not too many health professionals were willing to accept herbal medicin because there was no scientific acking to prove its effectivity. It s only now that they are starting to appreciate the usefulness of herbal medicine," she said.

Considering that about one-third the population, particularly in rucine, and since they grow in abundance in many areas in and around the country we felt it is high time to develop herbal medicine."

The DoST has almost a hundred plants for scientific validation in terms of safety and efficacy. Dr. Zara says the preparation adheres to the World Health Organization (WHO) criteria for strict quality control standards, apart from the other tests and evaluation conducted by the NIRPROMP.

Since herbal medicine is currently generating awareness globally, Dr. Zara believes Filipinos are likely to adopt it as well. "I think it has a bright future here, specially so with its scientific backing. What we are hoping is for us to develop our own so as not be dependent on imported herbal medications."

Herbal medicine is actually part of the DoST's various programs since 1877. In fact, it has presented several of its products that were ready for transfer in conventions and seminars attended by students, health professionals and pharmaceutical companies. One of the companies which responded to its herbal medicine products was Pascual Laboratories Inc. (PLI).

As one of the leading pharmaceutical companies in the country the PLI introduced its two herbal products — *Ascof* (Lagundi) and *Re-Leaf* (Sambong) — the first herbal medicines licensed by the PCHRD. They are doing very well in the market, according to Dr. Zara.

As herbal medicine becomes a significant part of every Filipino's health, the DoST, through the support of PLI, aims for advanced technology for more competitive herbal products.

"We will be evaluating the herbal medicine program to see if we are moving in the right direction. We have to know if we are dealing with

Malaya
ENTERTAINMENT

Thursday, April 15, 1999

LUCHI The other side of CRUZ-VALDEZ

LUCHI Cruz-Valdez is a popular broadcast journalist on GMA 7. Her typical day starts with taping her episode for "At Your Service," a regular segment in "GMA Network News" that tackles issues on health, parenting and consumer rights of the Filipinos. She is also part of the investigative team of "Brigade Siete" and the new full-length documentary, "I-Witness," (Mondays, 11 p.m.) where she shares the TV screen with Che-Che Lazaro, Mike Enriquez and Jessica Soho. On top of these, she also checks the scripts and oversees the production of "Saksi" and "GMA Network News" from Monday to Friday.

On television, she comes across as an intelligent and smart woman. Behind the camera, she is very hardworking. Her sense of humor gets her through the hectic day. All these attributes can be glimpse by televiewers as she delivers the news with passion. At the end of the day, Luchi comes home to the comfort of home. Not everyone is aware that Luchi is a happily married woman blessed with two precocious boys. She is a devoted mother to her children. As with any working mother, she finds it hard to balance her career and her vocation. "I balance with great difficulty. I wish I could say that I am a fantastic time manager," says Luchi.

She makes it a point to keep her weekends free for her family. "I make no appointments on weekends so that we can go out town whenever we have the budget. Other times we just go to the malls to watch a movie or dine out," she adds.

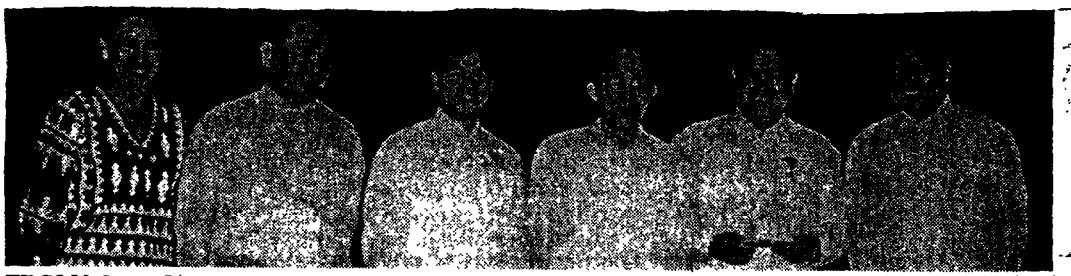
Like any typical mom and wife, she worries when her children and husband get sick. Whenever the common cough strikes, she gives them Ascof-Forte. "I go for natural things like Ascof Forte, a tablet for cough and asthma. The *lagundi* plant is a shrub with a five-leaf cluster known to cure asthma and cough. I believe in the product, that's why I decided to endorse Ascof Forte. I find it a refreshing alternative to the regular synthetic cough and asthma medicine. It's about time somebody put some science into herbal medicine and PLI/Altermed is doing the right thing in manufacturing herb-based medicine," says Luchi.

In the coming years, the market is expected to expand as scientific proof of the efficacy and safety of the herbs convince the medical community. No less than the World Health Organization recognizes and encourages the use of herbal medicine. It is estimated that 80% of the world's population relies on plant-based medicine for primary health care.

With these developments, Luchi did the right decision to endorse Ascof Forte. The product is scientifically researched and clinically proven for more than 20 years, as conducted by the National Integrated Research Program on Medicinal Plants (NIRPROMP). In fact, Ascof Forte does not have the usual side effects such as drowsiness, tremors and palpitation which are caused by taking the usual cough and asthma medicines.

PHILIPPINE DAILY INQUIRER

MONDAY, AUGUST 10, 1998



FROM left are Citem executive director Araceli Pinto Mansor, Trade and Industry Undersecretary Jose Juliano, Altermed Corp. product manager Nikky Nicandro III, Bangko Sentral ng Pilipinas Deputy Governor Edgardo Zialcita, Pascual Laboratories/Altermed Corp. president Dr. Abraham Pascual and former DTI secretary Cesar Bautista.

Pascual Lab, Altermed Corp. receive Rising Star citation

Pascual Laboratories Inc. and Altermed Corp. made headlines in the local setting as one of the recipients of the Rising Star citation at the 1997 Golden Shell Awards.

For the first time, a pharmaceutical company made it to the elite list of companies singled out by the Department of Trade and Industry as having an innovative product that shows a lot of promise in the international arena.

The Rising Start Citation award is given to companies which promote new products for export that exhibit tremendous potential to make it big in the international market.

PLI/Altermed is being cited for pioneering the production and marketing of indigenous herbal medicines—Ascof (Lagundi) which is an alternative natural remedy for cough or asthma and Re-Leaf (Sambong) the dissolution of kidney stones and as a potassium-sparing diuretic for people with mild to moderate congestive heart failure and edema.

DTI considers this endeavor as a remarkable move toward the global arena of the export industry—product of Filipino ingenuity, proudly Philippine made.

PLI/Altermed aims to make herbal medicines fully integrated into mainstream healthcare. The company is pulling all stops to make their mark in the pharmaceutical industry via these natural medicines.

Giving them an edge is their ability to manufacture these into modern and convenient tablet forms based on CGMP standards. Thanks to the growing support of medical practitioners health-conscious individuals and strategic marketing support provided by Pharex Healthcare Corp. Altermed is gaining stronger public acceptance and usage for its herbal medicines. The company is also laying the groundwork for exporting these to different parts of the world.

HEALTH NEWS

SEPTEMBER 21, 1998

Herbal Medicines Health Express

TODAY, consumers become more conscious about the food they eat and the medicine they take. They focus on the basic and simple way of living. They prefer organic food that are not smeared with pesticides and herbal medicine that keep the natural ingredients intact. An offshoot of this preference is the upswing demand for herbal medicines.

One store that recognized this upswing trend is Health Express. Its owner, Mrs. Rosalie Wells, pioneered the idea of carrying locally made herbal medicine in all her health store branches. Currently, she has two herbal medicine Ascof and Re-lef, that aggressively sell in the shelves.

Both Ascof and Re-leaf are the first of its kind currently marketed in the country. Ascof is for the relief of mild to moderate bronchial asthma and cough while Re leaf is a potent remedy for kidney stone dissolution. It is also used as a diuretic medicine for those with mild to moderate congestive heart failure or edema.

Health Express started in 1990 when people are just beginning to discover health food and health products. "Now people are very interested in vitamins, herbs and all these natural things. Our customers come from all walks of life, young and old. "I'm surprised that young people are interested in body building. High schools kids come here, they want to know how they can improve their body. It is okay for them to take multi-vitamins. But we don't tell them right away to buy this or that product. Our pharmacists advise them to start slowly. We guide them when they buy. We consult our books and ask our suppliers for production information so we can explain better to the customers what these products are for" says Mrs. Wells.

"Ascof and Re-leaf are world class products. I remember when I went to a convention in Anaheim, California, I brought these products of Altermed. People were impressed with the packaging. The Altermed products can compete with the imported brands," says Mrs. Wells.

Ascof and Re-leaf show a lot of promise in the international market. In fact, Altermed won the Rising Star Citation Award given by the Department of Trade and Industry (DTI) in the recently concluded 1997 Golden Shell Awards which recognizes companies who promote winning products for export. Altermed is cited for pioneering the production and marketing of indigenous herbal medicines. They have become the first pharmaceutical company to be recognized by the Department of Trade and Industry. Global recognition also came to the New techniques and Products in Geneva, Switzerland last April 1997. It is the highest recognition ever received by our country in the past twenty five years history of this international exhibition. Right now, the company is also laying the groundwork for exporting Ascof and Re-leaf to different countries around the world.

alaya
LIVING
Tuesday, October 13, 1998

La Niña

A season of cough, colds, asthma

THE rainy season may usher in a fresher and cleaner environment, but it also signals the beginning of a particular period when certain diseases become more prevalent or to a some extent may even reach epidemic proportions.

The "La Nina" phenomenon and its effects will become more evident as we experience an increasing incidence of Cough, Colds and Asthma. Knowing more about these diseases is the first step keeping ourselves and our family healthy. As the saying goes, "an ounce of prevention is worth much more than a pound of cure."

The common colds, cough

The colds are mainly due to viruses that enter the body and overwhelm its defense mechanisms. These viruses are transmitted through the air from one person to another. Symptoms include a combination of cough, headache, fever, watery/congested eyes and nose, sore throat, chill and muscle pains. Sometimes, it may be sever enough to knock us down for a few days, but often we really don't feel that bad that we can still report to work in spite of the discomfort we experience. Thus, instead of containing, the spread of the virus, we perpetuate it by passing it on to our officemates or fellow commuters.

Despite the rapid technological advances in modern medicine, there is still no cure for common cold. It is good therefore that Nature designed common colds to be self-limiting and thus resolve by itself within a few days (although a few strains are more virulent with a longer recovery period). To avoid catching a cold, eat plenty of vegetables and fruits, exercise regularly, take Vitamin C (Poten-Cee) 500 mg. per day (during the season), avoid people with colds and minimize your exposure in crowded enclosures.

Asthma

To many people, the rainy season is also Asthma season. It is during this time that the number of fungal spores in the air is more abundant and live longer due to the relatively higher level of moisture in the air. It is also during this period that flowers bloom and release their pollen in the air. These coupled with temperature fluctuations and pollution in external environment, stress from work and greater exposure to the common cold virus, greatly predisposes an asthmatic to a major attack. Symptoms may include difficulty in breathing, expiratory wheezing, cough and anxiety.

Like the common cold, there is still no real cure for asthma. Treatment is largely aimed at controlling in the inflammation, bronchodilation or both. To prevent an attack, asthmatics should avoid getting too tired, stay indoors in an air-conditioned room with a bio-filter, avoid crowded places.

Natural remedy

However, should you be unfortunate enough to be put down by cough, colds and asthma, there is now an available natural cough and asthma remedy. Ascof (Lagundi) is the first licensed herbal medicine in the Philippines. It is an effective cough remedy and anti-asthma medication without the usual side effects which you may experience with your regular medicines. It has won recognitions both locally and internationally which is a milstone for the pharmaceutical industry. It is a safe and effective way of relieving you of the discomforts of the cold season. For more information you may call Alternea Hotline at 411-9907/924-2158 or 70.

PEOPLE'S JOURNAL
Everybody's Newspaper
Vol. XX, No.321 Saturday, October 24, 1998

Preparing for the season of colds, cough and asthma

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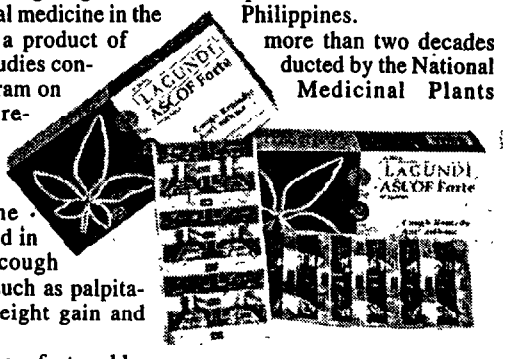
New asthma drug in market

Ascof Forte (Lagundi) tablet, the first and only all-Filipino drug for asthma and cough is now available in major drugstores nationwide. It is the first and only Bureau of Food and Drugs-registered and Department of Science and Technology-licensed herbal medicine in the Philippines.

Ascof Forte tablet is a product of more than two decades of research and clinical studies conducted by the National Integrated Research Program on Medicinal Plants (NIRPROMP). Studies revealed that Ascof Forte has a wide margin of safety and efficacy. Ascof Forte does not have the common side effects found in the regular asthma and cough medicines in the market such as palpitation, tremors, anxiety, weight gain and drowsiness.



Ascof Forte is being manufactured by Pascual Laboratories and marketed by Altermed Corp. and Pharex Healthcorp. For inquiries, please call Altermed hotline - 4119907/9242158 or 70.

CLINIC TALK

Filipino cough medicine

Department of Science and Technology Secretary Filemon Uriarte Jr. shows off a packet of Lagundi, an all-Filipino-made cough medicine during his keynote address on the occasion of Philexport's recent general membership meeting held at Century Park Hotel in Manila. Uriarte batted for stronger partnership between the science community and industry to spur economic expansion. Lagundi was developed by DOST's Philippine Council for Health Research and Development and currently manufactured and distributed as Ascof (brand name) through a license agreement with Pascual Laboratories. (S&T Media Service)

Herbal tablets enter P59 B pharmaceutical industry

SAMBONG and lagundi have joined the country's P59 billion pharmaceutical industry.

Sambong-based tablets are prescribed for patients with normal kidney function but who have urinary tract stones. As diuretic, they may also be prescribed for mild to moderate congestive heart failure and edema. It is the first licensed herbal anti-urolithiasis and diuretic in the Philippines.

Lagundi-based tablets are prescribed for the relief of cough due to common cold, flu, and mild to moderate acute bronchitis. They may also be prescribed for the relief of reversible, mild to moderate bronchospasm in adults and children at least two years old with obstructive airway disease such as asthma, chronic bronchitis, and other broncho-pulmonary disorders.

According to researchers, both tablets have passed the World Health Organization (WHO) prescribed tests for establishing safety and efficacy of medicinal plants.

The suggested retail price of each 250 milligram sambong tablet - marketed under the brand name Re-Leaf — is P1.80. A 250 mg. lagundi tablet — marketed as Ascof — costs P1.50. They are manufactured by Pascual Laboratories, the first and only private Filipino pharmaceutical company duly licensed by the Bureau of Food and Drugs to produce herbal medicines in tablet form.

Two other drug companies will market the sambong and lagundi tablets but have yet to get approval from BFAD.

The technology in developing sambong is the product of over a decade of research — for lagundi, more than two decades — by the National Integrated Research Program on Medicinal Plants, a consortium of the country's top academic institutions and scientists. Research and development were mostly undertaken by the University of the Philippines Manila, University of the Philippines Los Baños, and the Philippine Council for Health Research and Development, an agency of the Department of Science and Technology.

"We're very optimistic about these products," says Dr. Abraham F. Pascual, president of Pascual Laboratories. "We would be happy if we can get point one percent of the market". He estimates the cough medication market alone is worth around P1.5 to P2 billion.

Government surveys also show that 68 percent of doctors are aware of scientific studies on herbal medicine. Some 50 percent of doctors are also aware of the medicinal properties of sambong and lagundi. MNC

Herbal medicines for asthma, kidney stones promoted

WHEN asthma attacks become more frequent or kidney stones get in the way of a healthy system, herbal medicine presents itself as an effective alternative medicine. As new studies reveal, certain herbs can readily provide the cures.

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Herbal medicine is actually part of the DOST's various programs since 1877. In fact, it has presented several of its products that were ready for transfer in conventions and seminars attended by students, health professionals and pharmaceutical companies. One of the companies which responded to its herbal medicine products was Pascual Laboratories Inc.

As one of the leading pharmaceutical companies in the country, the PLI introduced its two herbal products—Ascof (lagundi) and Releaf (sambong)—the first herbal medicines licensed by the PCHRD. They are doing very well in the market, according to Dr. Zara.

As herbal medicine becomes a significant part of every Filipino's health, the DOST, through the support of PLI, aims for advanced technology for more competitive herbal products.

"We will be evaluating the herbal medicine program to see if we are moving in the right direction. We have to know if we are dealing with the right plants or if our management system works. With these herbal medicines doing very well in the market, we hope to develop more herbal medicines in the future," Dr. Zara said.